	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	312	(ancylosoma adj duodenale) or (anclostoma adj ceyanicum) or (necator adj americanus) or (ancylostoma adj caninum)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/12 16:26			0
2	BRS	L2	42	(polypeptide or peptide or protein) same 1	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:27			0
3	BRS	L3	21632	inhibit$3 same platelet	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:28			0
4	BRS	L4	1	2 same 3	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:29			0
5	BRS	L6	34	hookworm same 2	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:29			0
6	BRS	L7	1	6 same 3	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:29			0
7	BRS	L8	8642	integrin	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:29			0
8	BRS	L9	55287	fibrinogen or collagen	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:30			0
9	BRS	L10	1666	8 same 9	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:30			0
10	BRS	L11	0	6 same 10	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:31			0
11	BRS	L12	31584	epinephrine or thrombin or adp	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:31			0
12	BRS	L13	3742	3 same 12	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:32			0
13	BRS	L14	0	13 same 6	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:32			0
14	BRS	L15	39620	immune adj response	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:33			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
15	BRS	L16	2	15 same 6	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:34			0
16	BRS	L18	0	chadderdon adj robert.in.	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:36			0
17	BRS	L19	0	del adj valle adj antonio.in.	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:36			0
18	BRS	L20	0	harrison adj lisa.in.	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:36			0
19	BRS	L17	3	cappello adj michael.in.	USPAT; US-PGPUB; EPO; JPO;	2003/09/12 16:37			0

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FILE 'MEDLINE' ENTERED AT 16:46:56 ON 12 SEP 2003

FILE 'CAPLUS' ENTERED AT 16:46:56 ON 12 SEP 2003
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FILE 'AGRICOLA' ENTERED AT 16:46:56 ON 12 SEP 2003

=> s hookworm
L1        8048 HOOKWORM

=> s l1 (p) (peptide polypeptide or protein)
L2         501 L1 (P) (PEPTIDE POLYPEPTIDE OR PROTEIN)

=> s (ancylostoma adj duodenate) or (ancylostoma ceylanicum) or (necator americanus) or (ancylosto
L3        4739 (ANCYLOSTOMA ADJ DUODENATE) OR (ANCYLOSTOMA CEYLANICUM) OR (NECA
               TOR AMERICANUS) OR (ANCYLOSTOMA CANINUM)

=> s l3 (p) (PEPTIDE POLYPEPTIDE OR PROTEIN)
L4         470 L3 (P) (PEPTIDE POLYPEPTIDE OR PROTEIN)

=> s l4 or l2
L5         728 L4 OR L2

=> s inhibit? (p) platelet
L6      165396 INHIBIT? (P) PLATELET

=> s l5 (p) l6
L7          16 L5 (P) L6

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8             8 DUPLICATE REMOVE L7 (8 DUPLICATES REMOVED)

=> d l8 1-8 ibib abs

L8   ANSWER 1 OF 8     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2003321665     MEDLINE
DOCUMENT NUMBER:    22735468   PubMed ID: 12850261
TITLE:              Isolation and molecular cloning of a secreted hookworm
                    platelet inhibitor from adult Ancylostoma caninum.
AUTHOR:             Del Valle Antonio; Jones Brian F; Harrison Lisa M;
                    Chadderdon Robert C; Cappello Michael
CORPORATE SOURCE:   Department of Pediatrics, Yale University School of
                    Medicine, 464 Congress Avenue, New Haven, CT 06520-8081,
                    USA.
CONTRACT NUMBER:    HD007388 (NICHD)
SOURCE:             MOLECULAR AND BIOCHEMICAL PARASITOLOGY, (2003 Jul) 129 (2)
                    167-77.
                    Journal code: 8006324. ISSN: 0166-6851.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200309
ENTRY DATE:         Entered STN: 20030710
                    Last Updated on STN: 20030909
                    Entered Medline: 20030908
AB     ***Hookworms***  , bloodfeeding intestinal nematodes, are a leading
     cause of iron deficiency anemia in the developing world.  These parasites
     have evolved potent mechanisms of interfering with mammalian hemostasis,
     presumably for the purpose of facilitating bloodfeeding.  Adult
       ***Ancylostoma***     ***caninum***   worm extracts contain an activity
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that ***inhibits*** ***platelet*** aggregation and adhesion by blocking the function of two cell surface integrin receptors, glycoprotein IIb/IIIa and GPIa/IIa. Using rpHPLC, the ***hookworm*** ***platelet*** ***inhibitor*** activities have been purified from ***protein*** extracts of A. caninum. Because the two ***inhibitory*** activities co-purified through multiple chromatographic steps, have similar molecular masses and share identical N-terminal as well as internal amino acid sequence homology, it is likely that they represent a single gene product. A cDNA corresponding to the purified ***hookworm*** ***platelet*** ***inhibitor*** (HPI) ***protein*** has been cloned from adult A. caninum RNA, and the translated amino acid sequence shows significant homology to Neutrophil ***Inhibitory*** Factor and Ancylostoma Secreted ***Proteins*** , suggesting that these related ***hookworm*** ***proteins*** represent a novel class of integrin receptor antagonists. Polyclonal antibodies raised against the recombinant HPI ***protein*** recognize corresponding native ***proteins*** in A. caninum extracts and excretory/secretory products, and immunohistochemistry data have identified the cephalic glands as the major source of the ***inhibitor*** within the adult ***hookworm*** . These data suggest that HPI is secreted by the adult stage of the parasite at the site of intestinal attachment. As such, it may represent a viable target for a vaccine-based strategy aimed at interfering with ***hookworm*** -induced gastrointestinal hemorrhage and iron deficiency anemia.

L8 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:615867 CAPLUS
DOCUMENT NUMBER: 137:165271
TITLE: Integrin-binding fusion proteins of dendroaspin and anticoagulant proteins and their use in the treatment of clotting disorders
INVENTOR(S): Lu, Xinjie; Kakkar, Vijay Vir
PATENT ASSIGNEE(S): Trigen Limited, UK
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002063017	A2	20020815	WO 2002-GB500	20020205

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-267234P P 20010205
OTHER SOURCE(S): MARPAT 137:165271
AB Fusion ***proteins*** of an integrin-binding ***protein*** , esp. dendroaspin and a second ***protein*** are described for use in the targeted therapeutic delivery of ***proteins*** to blood vessels. The second moiety of the fusion ***protein*** is most often an anticoagulant ***protein*** for use in the treatment of clotting disorders. Chimeric genes encoding a fusion ***proteins*** of dendroaspin and the proteinase ***inhibitor*** NAP5 of ***Ancylostoma*** ***caninum*** was constructed and expressed in Escherichia coli. The ***proteins*** ***inhibited*** ADP-induced ***platelet*** aggregation at concns. of 260-500 nm, compared to 76-277 nM for dendroaspin and other snake venom anticoagulants. They also ***inhibited*** collagen-induced ***platelet*** aggregation. Dendroaspin did not ***inhibit*** factor Xa, but the fusion ***proteins*** ***inhibited*** it at 1.1-140.9 nM.

L8 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:707193 CAPLUS
DOCUMENT NUMBER: 133:286422
TITLE: Hookworm platelet aggregation inhibitor
INVENTOR(S): Cappello, Michael; Chadderdon, Robert C.; Del Valle, Antonio; Harrison, Lisa M.
PATENT ASSIGNEE(S): Yale University, USA

SOURCE: PCT Int. Appl., 38 pp.
CODEN: P[redacted]D2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058341	A1	20001005	WO 2000-US8519	20000330
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165598	A1	20020102	EP 2000-918509	20000330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539817	T2	20021126	JP 2000-608041	20000330

PRIORITY APPLN. INFO.: US 1999-127239P P 19990331
WO 2000-US8519 W 20000330

AB An ***inhibitor*** of ***platelet*** aggregation and adhesion is purified and characterized from sol. ***protein*** exts. of adult ***Ancylostoma*** ***caninum*** ***hookworms*** and then cloned and sequenced. The ***inhibitor*** blocks ***platelet*** aggregation in response to a variety of agonists, interfering with the binding of at least one cell surface integrin with its resp. ligand. Embodiments include ***inhibition*** of the binding of fibrinogen to cell surface integrin GPIIb/IIIa (.alpha.IIb.beta.3) and ***inhibition*** of the binding of collagen to cell surface integrin GPIa/IIa (.alpha.2.beta.1). Medical and veterinary pharmaceutical and immunol. compns. contg. the ***platelet*** ***inhibitor*** , and methods of using it, are described.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:531682 CAPLUS
DOCUMENT NUMBER: 133:131741
TITLE: Serine proteinase inhibitors and anticoagulant proteins from Ancyclostoma caninum
INVENTOR(S): Vlasuk, George Phillip; Stanssens, Patrick Eric Hugo; Messens, Joris Hilda Lieven; Lauwereys, Marc Josef; Laroche, Yves Rene; Jespers, Laurent Stephane; Gansemans, Yannick Georges Jozef; Moyle, Matthew; Bergum, Peter W.
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: U.S., 199 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6096877	A	20000801	US 1999-249461	19990212

PRIORITY APPLN. INFO.: US 1999-249461 19990212
OTHER SOURCE(S): MARPAT 133:131741

AB ***Proteins*** which have activity as anticoagulants or serine protease ***inhibitors*** and have at least one NAP (nematode anticoagulant ***protein***) domain and are described. Certain of these ***proteins*** have factor Xa ***inhibitory*** activity and others have activity as ***inhibitors*** of factor VIIa/TF. These ***proteins*** can be isolated from natural sources such as the nematode Ancyclostoma caninum, chem. synthesized or made by expression of the cloned gene. Purifn. of two such ***proteins*** from A. caninum, cloning and expression of cDNAs encoding them, and use of the cDNAs to clone corresponding cDNAs from ***Necator*** ***americanus*** are described. The ***proteins*** had a Ki for factor Xa amidolytic activity of 43.+-.5 or 996.+-.65 pM and for prothrombin of 144.+-.15 and 207.+-.40 pM resp. The ***proteins*** were also effective in preventing thrombotic occlusion in vivo in the rat model of FeCl3-induced

platelet -dependent arterial thrombosis.
REFERENCE COUNT: 138 THERE ARE 138 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:492067 CAPLUS
DOCUMENT NUMBER: 133:116714
TITLE: Serine proteinase inhibitors and anticoagulant proteins from Ancyclostoma caninum
INVENTOR(S): Vlasuk, George Phillip; Stanssens, Patrick Eric Hugo; Messens, Joris Hilda Lieven; Lauwereys, Marc Josef; Laroche, Yves Rene; Jespers, Laurent Stephane; Gansemans, Yannick Georges Jozef; Moyle, Matthew; Bergum, Peter W.
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: U.S., 201 pp., Cont.-in-part of U.S. 5,872,098.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6090916	A	20000718	US 1997-809455	19970417
US 5945275	A	19990831	US 1994-326110	19941018
US 5863894	A	19990126	US 1995-465380	19950605
US 5866542	A	19990202	US 1995-486397	19950605
US 5866543	A	19990202	US 1995-486399	19950605
US 5872098	A	19990216	US 1995-461965	19950605
WO 9612021	A2	19960425	WO 1995-US13231	19951017
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MW, MX, NO, NZ, PL, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6534629	B1	20030318	US 1999-249473	19990212
US 2003113890	A1	20030619	US 2000-498272	20000204

PRIORITY APPLN. INFO.:
US 1994-326110 A2 19941018
US 1995-461965 A2 19950605
US 1995-465380 A2 19950605
US 1995-486397 A2 19950605
US 1995-486399 A2 19950605
WO 1995-US13231 W 19951017
US 1997-809455 A1 19970417

OTHER SOURCE(S): MARPAT 133:116714
AB ***Proteins*** which have activity as anticoagulants or serine protease ***inhibitors*** and have at least one NAP (nematode anticoagulant ***protein***) domain and are described. Certain of these ***proteins*** have factor Xa ***inhibitory*** activity and others have activity as ***inhibitors*** of factor VIIa/TF. These ***proteins*** can be isolated from natural sources such as the nematode Ancyclostoma caninum, chem. synthesized or made by expression of the cloned gene. Purifn. of two such ***proteins*** from A. caninum, cloning and expression of cDNAs encoding them, and use of the cDNAs to clone corresponding cDNAs from ***Necator*** ***americanus*** are described. The ***proteins*** had a Ki for factor Xa amidolytic activity of 43.+-.5 or 996.+-.65 pM and for prothrombin of 144.+-.15 and 207.+-.40 pM resp. The ***proteins*** were also effective in preventing thrombotic occlusion in vivo in the rat model of FeCl3-induced ***platelet*** -dependent arterial thrombosis.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999208706 MEDLINE
DOCUMENT NUMBER: 99208706 PubMed ID: 10191228
TITLE: The hookworm platelet inhibitor: functional blockade of integrins GPIIb/IIIa (alphaIIbbeta3) and GPIa/IIa (alpha2beta1) inhibits platelet aggregation and adhesion in vitro.
AUTHOR: Chadderdon R C; Cappello M
CORPORATE SOURCE: Dartmouth Medical School, Hanover, NH, USA.. robert.c.chadderdon@dartmouth.edu
CONTRACT NUMBER: AI-01299 (NIAID)

HD-27757 (NICHD)
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1999 May) 179) 1235-41.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990607

AB ***Hookworms*** , aggressive, blood-feeding, intestinal nematodes, are currently a leading cause of iron deficiency anemia in the developing world. An ***inhibitor*** of ***platelet*** aggregation and adhesion has been partially purified and characterized from soluble ***protein*** extracts of adult ***Ancylostoma*** ***caninum*** ***hookworms*** . This ***protein*** , named the ***hookworm*** ***platelet*** ***inhibitor*** , has an estimated molecular mass of 15 kDa as determined by size-exclusion chromatography. In addition to blocking ***platelet*** aggregation in response to a variety of agonists, the partially purified ***inhibitor*** also prevents adhesion of resting ***platelets*** to immobilized fibrinogen and collagen. ***Inhibitory*** monoclonal antibodies were used to identify specific blockade of cell surface integrins GPIIb/IIIa (alphaIIbbeta3) and GPIa/IIa (alpha2beta1), the ***platelet*** receptors for fibrinogen and collagen, respectively. This broad-spectrum anti- ***platelet*** activity is also present in excretory and secretory products of adult worms, suggesting a biologic role for the ***hookworm*** ***platelet*** ***inhibitor*** in vivo.

L8 ANSWER 7 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 97:795907 SCISEARCH
THE GENUINE ARTICLE: YC301
TITLE: Antithrombotic efficacy of a recombinant nematode anticoagulant peptide (rNAP5) in canine models of thrombosis after single subcutaneous administration
AUTHOR: Rebello S S; Blank H S; Rote W E; Vlasuk G P; Lucchesi B R (Reprint)
CORPORATE SOURCE: UNIV MICHIGAN, SCH MED, DEPT PHARMACOL, 1301C MED SCI RES BLDG 3, ANN ARBOR, MI 48109 (Reprint); UNIV MICHIGAN, SCH MED, DEPT PHARMACOL, ANN ARBOR, MI 48109
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (OCT 1997) Vol. 283, No. 1, pp. 91-99.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0022-3565.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 34
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We describe the antithrombotic effects of recombinant nematode anticoagulant peptide (rNAP5), a selective and direct factor Xa inhibitor, after a single s.c. administration in canine models of arterial and venous thrombosis. The systemic anticoagulant effects of rNAP5 were evaluated initially in conscious dogs after s.c. dosing (0.03, 0.1 and 0.3 mg/kg) that resulted in a dose-dependent increase in the activated clotting time and the activated partial thromboplastin time. The antithrombotic effects of rNAP5 were evaluated in anesthetized dogs where saline or rNAP5 (0.03, 0.1 and 0.3 mg/kg s.c.) was administered 1 hr before the left circumflex coronary artery was subjected to electrolytic injury. In the saline group (n = 10), the left circumflex artery occluded in 79 +/- 9 min, and 5 of 10 animals progressed to sudden death due to ventricular fibrillation. rNAP5 significantly prolonged the time to occlusion in the 0.03 mg/kg (163 +/- 62 min) and 0.1 mg/kg (327 +/- 62) treatment groups (n = 6). In the 0.3 mg/kg group (n = 5), all of the injured vessels remained patent for 8 hr. There was a dose-dependent reduction in the thrombus mass in the rNAP5-treated animals as compared with controls, as well as a lower mortality rate. rNAP5, in the doses of 0.03 and 0.1 mg/kg, did not alter the bleeding time, whereas 0.3 mg/kg produced a 5-fold increase. In a separate study, we evaluated the efficacy of rNAP5 (0.1 mg/kg) in the prevention of carotid artery and jugular vein thrombosis. In response to endothelial injury, the carotid artery and jugular vein in the saline group (n = 6) occluded in 142 +/- 16 and 100 +/- 11 min, respectively, compared with rNAP5, which maintained vessel patency in the carotid artery (6/6) and jugular vein (5/6) and significantly decreased the thrombus

weights. The results demonstrate that rNAP5 has antithrombotic efficacy in canine models of arterial and venous thrombosis after a single s.c. administration.

L8 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:33807 CAPLUS
DOCUMENT NUMBER: 122:1077
TITLE: Novel neutrophil inhibitors for use as inflammation inhibitors
INVENTOR(S): Moyle, Matthew; Foster, David Lee; Vlasuk, George Phillip
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9414973	A1	19940707	WO 1993-US12626	19931223
W: AU, CA, FI, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2152599	AA	19940707	CA 1993-2152599	19931223
AU 9460805	A1	19940719	AU 1994-60805	19931223
AU 694103	B2	19980716		
EP 682714	A1	19951122	EP 1994-907114	19931223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08505055	T2	19960604	JP 1993-515483	19931223

PRIORITY APPLN. INFO.:
US 1992-996972 A 19921224
US 1993-60433 A 19930511
US 1993-151064 A 19931110
WO 1993-US12626 W 19931223

AB Peptides that ***inhibit*** neutrophil activity including adhesion to vascular endothelial cells are described for use as anti-inflammatories with a greater specificity than prior art inflammation ***inhibitors*** . The peptides are derived from a glycoprotein of ***hookworm*** and may be manufd. by expression of the corresponding gene. Neutrophil ***inhibitors*** were purified 200-fold (12% yield) from lysates of canine ***hookworm*** by chromatog. on ConA-Sepharose, Superdex 200, ceramic hydroxyapatite and by reverse phase HPLC, or by a combination of ion-exchange chromatog., SDS-polyacrylamide gel electrophoresis, and isoelec. focussing. A cDNA was cloned by std. methods using amino acid sequence-derived primers to obtain a partial cDNA by PCR and the full-length cDNA expressed in COS-7 and CHO cells and in Pichia pastoris. The ***protein*** did not affect ADP-induced ***platelet*** aggregation. The primary receptor for the ***inhibitor*** was the CD11b/CD18. The neutrophil ***inhibitor*** was shown to have a protective effect on arachidonic acid-induced neutrophil infiltration into ear tissue in a rat model.

=> d his

(FILE 'HOME' ENTERED AT 16:46:33 ON 12 SEP 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 16:46:56 ON 12 SEP 2003
L1 8048 S HOOKWORM
L2 501 S L1 (P) (PEPTIDE POLYPEPTIDE OR PROTEIN)
L3 4739 S (ANCYLOSTOMA ADJ DUODENATE) OR (ANCYLOSTOMA CEYLANICUM) OR (N
L4 470 S L3 (P) (PEPTIDE POLYPEPTIDE OR PROTEIN)
L5 728 S L4 OR L2
L6 165396 S INHIBIT? (P) PLATELET
L7 16 S L5 (P) L6
L8 8 DUPLICATE REMOVE L7 (8 DUPLICATES REMOVED)

=> s integrin
L9 107326 INTEGRIN

=> s fibrinogen or collagen
L10 549752 FIBRINOGEN OR COLLAGEN

=> s l9 (p) l10
L11 17045 L9 (P) L10

```
=> s l8 (p) l11
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L76 (P) L67'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L78 (P) L68'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L82 (P) L70'
L12           3 L8 (P) L11

=> s epinephrine or thrombin or adp
L13      478318 EPINEPHRINE OR THROMBIN OR ADP

=> s l8 (p) l13
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L96 (P) L87'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L98 (P) L88'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L102 (P) L90'
L14           2 L8 (P) L13

=> s l1 (p) infection
L15        4859 L1 (P) INFECTION

=> s l8 (p) infection
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L116 (P) INFECTION'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L118 (P) INFECTION'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L122 (P) INFECTION'
L16           0 L8 (P) INFECTION

=> d his

     (FILE 'HOME' ENTERED AT 16:46:33 ON 12 SEP 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     16:46:56 ON 12 SEP 2003
L1          8048 S HOOKWORM
L2           501 S L1 (P) (PEPTIDE POLYPEPTIDE OR PROTEIN)
L3          4739 S (ANCYLOSTOMA ADJ DUODENATE) OR (ANCYLOSTOMA CEYLANICUM) OR (N
L4           470 S L3 (P) (PEPTIDE POLYPEPTIDE OR PROTEIN)
L5           728 S L4 OR L2
L6        165396 S INHIBIT? (P) PLATELET
L7            16 S L5 (P) L6
L8             8 DUPLICATE REMOVE L7 (8 DUPLICATES REMOVED)
L9        107326 S INTEGRIN
L10       549752 S FIBRINOGEN OR COLLAGEN
L11        17045 S L9 (P) L10
L12            3 S L8 (P) L11
L13       478318 S EPINEPHRINE OR THROMBIN OR ADP
L14            2 S L8 (P) L13
L15         4859 S L1 (P) INFECTION
L16            0 S L8 (P) INFECTION

=> s immune response
L17      377594 IMMUNE RESPONSE

=> s l17 and l8
L18            0 L17 AND L8

=> s cappello michael/au
L19           52 CAPPELLO MICHAEL/AU

=> s chadderdon robert/au
L20            0 CHADDERDON ROBERT/AU

=> s del valle antonio/au
L21            6 DEL VALLE ANTONIO/AU

=> s harrison lisa/au
L22           10 HARRISON LISA/AU

=> s l19 or l21 or l22
L23           61 L19 OR L21 OR L22
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=> s l23 and (l1 or l3)
L24          41 L23 AND (L1 OR L3)

=> s l24 and l6
L25           7 L24 AND L6

=> s l25 not l8
L26           5 L25 NOT L8

=> d l26 1-5 ibib abs

L26  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        2003:519414  CAPLUS
TITLE:                   Isolation and molecular cloning of a secreted
                           ***hookworm***  ***platelet***  ***inhibitor***
                         from adult  ***Ancylostoma***  ***caninum***
AUTHOR(S):               ***Del Valle, Antonio***  ; Jones, Brian F.;
                         Harrison, Lisa M.; Chadderdon, Robert C.;
                           ***Cappello, Michael***
CORPORATE SOURCE:        Child Health Research Center, Departments of
                         Pediatrics and Epidemiology & Public Health, Yale
                         University School of Medicine, 464 Congress Avenue,
                         New Haven, CT, 06520-8081, USA
SOURCE:                  Molecular and Biochemical Parasitology (2003), 129(2),
                         167-177
                         CODEN: MBIPDP; ISSN: 0166-6851
PUBLISHER:               Elsevier Science B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB     ***Hookworms***  , bloodfeeding intestinal nematodes, are a leading
     cause of iron deficiency anemia in the developing world.  These parasites
     have evolved potent mechanisms of interfering with mammalian hemostasis,
     presumably for the purpose of facilitating bloodfeeding.  Adult
       ***Ancylostoma***  ***caninum***  worm exts. contain an activity that
       ***inhibits***  ***platelet***  aggregation and adhesion by blocking
     the function of two cell surface integrin receptors, Glycoprotein IIb/IIIa
     and GPIa/IIa.  Using rpHPLC, the  ***hookworm***  ***platelet***
       ***inhibitor***  activities have been purified from protein exts. of A.
     caninum.  Because the two  ***inhibitory***  activities co-purified
     through multiple chromatog. steps, have similar mol. masses and share
     identical N-terminal as well as internal amino acid sequence homol., it is
     likely that they represent a single gene product.  A cDNA corresponding to
     the purified  ***hookworm***  ***platelet***  ***inhibitor***
     (HPI) protein has been cloned from adult A. caninum RNA, and the
     translated amino acid sequence shows significant homol. to Neutrophil
       ***Inhibitory***  Factor and Ancylostoma Secreted Proteins, suggesting
     that these related  ***hookworm***  proteins represent a novel class of
     integrin receptor antagonists.  Polyclonal antibodies raised against the
     recombinant HPI protein recognize corresponding native proteins in A.
     caninum exts. and excretory/secretory products, and immunohistochem. data
     have identified the cephalic glands as the major source of the
       ***inhibitor***  within the adult  ***hookworm***  .  These data suggest
     that HPI is secreted by the adult stage of the parasite at the site of
     intestinal attachment.  As such, it may represent a viable target for a
     vaccine-based strategy aimed at interfering with  ***hookworm***
     -induced gastrointestinal hemorrhage and iron deficiency anemia.

L26  ANSWER 2 OF 5  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        1999:316370  CAPLUS
DOCUMENT NUMBER:         131:127426
TITLE:                   The  ***hookworm***  ***platelet***
                           ***inhibitor***  : functional blockade of integrins
                         GPIIb/IIIa (.alpha.IIb.beta.3) and GPIa/IIa
                         (.alpha.2.beta.1)  ***inhibits***  ***platelet***
                         aggregation and adhesion in vitro
AUTHOR(S):               Chadderdon, Robert C.;  ***Cappello, Michael***
CORPORATE SOURCE:        Dept. of Pediatrics, Yale School of Medicine, New
                         Haven, CT, 06520-8081, USA
SOURCE:                  Journal of Infectious Diseases (1999), 179(5),
                         1235-1241
                         CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER:               University of Chicago Press
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB     ***Hookworms***  , aggressive, blood-feeding, intestinal nematodes, are
     currently a leading cause of iron deficiency anemia in the developing
     world.  An  ***inhibitor***  of  ***platelet***  aggregation and
```

adhesion has been partially purified and characterized from sol. protein exts. of adult ***Ancylostoma*** ***caninum*** ***hookworms*** . This protein, named the ***inhibitor*** , has an estd. mol. mass of 15 kDa as detd. by size-exclusion chromatog. In addn. to blocking ***platelet*** aggregation in response to a variety of agonists, the partially purified ***inhibitor*** also prevents adhesion of resting ***platelets*** to immobilized fibrinogen and collagen. ***Inhibitory*** monoclonal antibodies were used to identify specific blockade of cell surface integrins GPIIb/IIIa (.alpha.IIb.beta.3) and GPIa/IIa (.alpha.2.beta.1), the ***platelet*** receptors for fibrinogen and collagen, resp. This broad-spectrum anti- ***platelet*** activity is also present in excretory and secretory products of adult worms, suggesting a biol. role for the ***hookworm*** ***platelet*** ***inhibitor*** in vivo.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:407712 BIOSIS
DOCUMENT NUMBER: PREV200300407712
TITLE: Isolation and molecular cloning of a secreted ***inhibitor*** ***platelet*** ***hookworm*** from adult ***Ancylostoma*** ***caninum*** .
AUTHOR(S): ***Del Valle, Antonio*** ; Jones, Brian F.; Harrison, Lisa M.; Chadderdon, Robert C.; ***Cappello, Michael*** (1)***
CORPORATE SOURCE: (1) Departments of Pediatrics and Epidemiology and Public Health, Child Health Research Center, Yale University School of Medicine, 464 Congress Avenue, New Haven, CT, 06520-8081, USA: michael.cappello@yale.edu USA
SOURCE: Molecular & Biochemical Parasitology, (July 2003, 2003) Vol. 129, No. 2, pp. 167-177. print.
ISSN: 0166-6851.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Hookworms*** , bloodfeeding intestinal nematodes, are a leading cause of iron deficiency anemia in the developing world. These parasites have evolved potent mechanisms of interfering with mammalian hemostasis, presumably for the purpose of facilitating bloodfeeding. Adult ***Ancylostoma*** ***caninum*** worm extracts contain an activity that ***inhibits*** ***platelet*** aggregation and adhesion by blocking the function of two cell surface integrin receptors, Glycoprotein IIb/IIIa and GPIa/IIa. Using rpHPLC, the ***hookworm*** ***platelet*** ***inhibitor*** activities have been purified from protein extracts of A. caninum. Because the two ***inhibitory*** activities co-purified through multiple chromatographic steps, have similar molecular masses and share identical N-terminal as well as internal amino acid sequence homology, it is likely that they represent a single gene product. A cDNA corresponding to the purified ***hookworm*** ***platelet*** ***inhibitor*** (HPI) protein has been cloned from adult A. caninum RNA, and the translated amino acid sequence shows significant homology to Neutrophil ***Inhibitory*** Factor and Ancylostoma Secreted Proteins, suggesting that these related ***hookworm*** proteins represent a novel class of integrin receptor antagonists. Polyclonal antibodies raised against the recombinant HPI protein recognize corresponding native proteins in A. caninum extracts and excretory/secretory products, and immunohistochemistry data have identified the cephalic glands as the major source of the ***inhibitor*** within the adult ***hookworm*** . These data suggest that HPI is secreted by the adult stage of the parasite at the site of intestinal attachment. As such, it may represent a viable target for a vaccine-based strategy aimed at interfering with ***hookworm*** -induced gastrointestinal hemorrhage and iron deficiency anemia.

L26 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:269953 BIOSIS
DOCUMENT NUMBER: PREV199900269953
TITLE: The ***Hookworm*** ***Platelet*** ***Inhibitor*** blocks fibrinogen binding to the ***platelet*** integrin GPIIb/IIIa (alphaIIbbeta3.
AUTHOR(S): ***Del Valle, Antonio (1)*** ; Chadderdon, Robert C. (1); ***Cappello, Michael (1)***
CORPORATE SOURCE: (1) Dept. of Pediatrics, Yale University School of Medicine, New Haven, CT USA
SOURCE: Pediatric Research, (April, 1999) Vol. 45, No. 4 PART 2, pp. 160A.
Meeting Info.: Annual Meeting of the American Pediatric

Society and the Society for Pediatric Research San Francisco, California, USA May 1-4, 1999
ISSN: 0031-3998.

DOCUMENT TYPE: Conference
LANGUAGE: English

L26 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:257895 BIOSIS
DOCUMENT NUMBER: PREV199900257895
TITLE: The ***hookworm*** ***platelet*** ***inhibitor*** : Functional blockade of integrins GPIIb/IIIa (alphaIIbbeta3) and GPIa/IIa (alpha2beta1) ***inhibits*** ***platelet*** aggregation and adhesion in vitro.

AUTHOR(S): Chadderdon, Robert C.; ***Cappello, Michael (1)***
CORPORATE SOURCE: (1) Dept. of Pediatrics, Yale School of Medicine, New Haven, CT, 06520-8081 USA

SOURCE: Journal of Infectious Diseases, (May, 1999) Vol. 179, No. 5, pp. 1235-1241.
ISSN: 0022-1899.

DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB ***Hookworms*** , aggressive, blood-feeding, intestinal nematodes, are currently a leading cause of iron deficiency anemia in the developing world. An ***inhibitor*** of ***platelet*** aggregation and adhesion has been partially purified and characterized from soluble protein extracts of adult ***Ancylostoma*** ***caninum*** ***hookworms*** . This protein, named the ***hookworm*** ***platelet*** ***inhibitor*** , has an estimated molecular mass of 15 kDa as determined by size-exclusion chromatography. In addition to blocking ***platelet*** aggregation in response to a variety of agonists, the partially purified ***inhibitor*** also prevents adhesion of resting ***platelets*** to immobilized fibrinogen and collagen. ***Inhibitory*** monoclonal antibodies were used to identify specific blockade of cell surface integrins GPIIb/IIIa (alphaIIbbeta3), and GPIa/IIa (alpha2beta1), the ***platelet*** receptors for fibrinogen and collagen, respectively. This broad-spectrum anti- ***platelet*** activity is also present in excretory and secretory products of adult worms, suggesting a biologic role for the ***hookworm*** ***platelet*** ***inhibitor*** in vivo.

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     (FILE 'HOME' ENTERED AT 16:46:33 ON 12 SEP 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     16:46:56 ON 12 SEP 2003
L1          8048 S HOOKWORM
L2           501 S L1 (P) (PEPTIDE POLYPEPTIDE OR PROTEIN)
L3          4739 S (ANCYLOSTOMA ADJ DUODENATE) OR (ANCYLOSTOMA CEYLANICUM) OR (N
L4           470 S L3 (P) (PEPTIDE POLYPEPTIDE OR PROTEIN)
L5           728 S L4 OR L2
L6        165396 S INHIBIT? (P) PLATELET
L7            16 S L5 (P) L6
L8             8 DUPLICATE REMOVE L7 (8 DUPLICATES REMOVED)
L9        107326 S INTEGRIN
L10       549752 S FIBRINOGEN OR COLLAGEN
L11        17045 S L9 (P) L10
L12            3 S L8 (P) L11
L13       478318 S EPINEPHRINE OR THROMBIN OR ADP
L14            2 S L8 (P) L13
L15         4859 S L1 (P) INFECTION
L16            0 S L8 (P) INFECTION
L17       377594 S IMMUNE RESPONSE
L18            0 S L17 AND L8
L19           52 S CAPPELLO MICHAEL/AU
L20            0 S CHADDERDON ROBERT/AU
L21            6 S DEL VALLE ANTONIO/AU
L22           10 S HARRISON LISA/AU
L23           61 S L19 OR L21 OR L22
L24           41 S L23 AND (L1 OR L3)
L25            7 S L24 AND L6
L26            5 S L25 NOT L8

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